Brain AVM Embolization. Retrospective Study Concerning 728 Patients Followed between 1984 and 2004

L. PICARD, S. BRACARD, R. ANXIONNAT, A. LEBEDINSKY, S. FINITSIS

Department of Diagnostic and Therapeutic Neuroradiology, University Neurologic Hospital; Nancy, France

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Introduction

This retrospective analysis concerns only patients who referred to the Diagnostic and Therapeutic Neuroradiology Department of the University Hospital of Nancy, followed-up and treated between 1984 and 2005 i.e. over the 20 last years. On purpose, we did not take into account numerous patients treated between 1970 and 1984; indeed, during this period, patients were treated with techniques and various technical processes now obsolete: embolizations using particles of varied nature or embolizations carried out by using small balloon metering jet microcatheters. These techniques, acceptable at the time of hyperselective catheterisation development, have now been abandoned and replaced by intranidal embolization. It is since 1984 that, in collaboration with Professor Jacques Moret, we decided to perform exclusively intranidal embolizations for the treatment of intracerebral arteriovenous malformations. The continuing improvement of materials made it possible to progressively obtain technical consistency thus making it possible to carry out more homogeneous series and consequently more valid comparisons.

Population concerned

The recruitment of the patients treated in the Department of Diagnostic and Therapeutic Neuroradiology at the University Hospital of Nancy deserves to be clarified because it explains the specificity of this population. Indeed, until 1995, more than 60% of patients presenting an intracerebral arteriovenous malformation were addressed to the Department by foreign neurosurgical teams. Obviously, these neurosurgical teams preferred to treat by themselves patients presenting arteriovenous malformations considered as simple i.e. small and located in non eloquent cerebral territories. This explains why the percentage of large arteriovenous malformations, located in highly functional zones, seems particularly significant in our population. During the 10 last years, the percentage of foreign patients has gradually dropped to stabilize around 33% of patients referred for an arteriovenous malformation.

The studied population includes 728 patients with an increased male prevalence: 57% men and 43 % women. The date of the first symptom varies significantly from 1 year to 84 years with an average age of 29 years. The average age of the first therapeutic intervention is delayed compared to the age of initial diagnosis. This age is 32 years with a minimum of two years and a maximum of 69 years. This shows, that on average, the patients are taken in charge within only three years after the occurence of the first symptom and that, with the exception of cases urgently addressed because of severe haemorrhage, no patient was taken in charge after the age of 69. It is important to notice that this attitude is completely different

than the one adopted for intracranial aneurysms, since, in our team, some fortuitously discovered aneurysms may be taken in charge even after the age of 80.

Initial clinical presentation

Patients presenting a severe hemorrhage as the initial symptom, often require an urgent neurosurgical intervention with decompression: thus they were not included in this work. Indeed, no arteriovenous malformation was embolized in the urgent setting nor during the acute hemorrhagic period.

Initial clinical presentation will be described by order of importance.The most frequent revealing symptom remains *intracerebral haemorrhage which occured in* 37,6% *of cases*. This symptom does not always lead to a therapeutic intervention since many patients are addressed to us only after the second or even sometimes the third haemorrhagic episode. Moreover it is important to note the frequency of intraventricular hemorrhage, which is often well tolerated, since once the acute period has passed, the patient often remains free of symptoms.

Epilepsy is the revealing symptom in 34% *of cases* corresponding to 249 patients out of 728. Of course epilepsy is primarily encoutered in cortical localizations: it is the first symptom in a little more than 50% of cases of frontal localizations (77 of 144, i.e. 55% of cases), parietal (87 of 180, ie. 48% of cases) and temporal (60 of 132 i.e. 45% of cases). Only occipital localizations escape this rule: 8 epilepsies of 65, i.e. 12% of cases.

Headache is paradoxically much less frequent since only 112 patients out of 728 had their malformation revealed because of it, corresponding to 15,4% cases. Headache associated with an intracerebral arteriovenous malformations has no particular clinical character: it may be episodical without any precise topography or even present as true migraines associated or not. Its localization has no topographic relationship to the localization of the malformation. Malformation related headache may relatively frequently be invalidating and may by itself constitute the essential element for a therapeutic indication. It should be noticed that very often embolization is quickly followed by a reduction of the intensity and frequency of headache.

Progressive neurological functional deficits are rare. Generally it is an insidiously appearing pyramidal syndrome of irritating type followed by a gradually invalidating motor deficit. Neurological deficits revealed the malformation in 7,1% *of cases* (52 of 728); more frequently they are associated with deep locations of the malformation representing 16,6% of cases. For many years, these progressive neurological deficits were thought to result from hemodynamic steal since, in a considerable number of cases, progressive reduction of the malformation resulted in a progressive deficit improvement. Currently, it seems that such deficits are primarily related to circulatory insufficiency secondary to venous hyperpression created by the arteriovenous malformation.

Fortuitous discoveries are the least frequent. During the 21 years studied, fortuitious discovery *represents only* 5,8% *of cases* i.e. 42 cases of 728. It should however be noticed that during last years, the increased use of ultrasound and brain MRI resulted in an indisputable increase of fortuitous discoveries of arteriovenous malformations.

Therapeutic indication

Therapy was always indicated after one or sometimes several consultations, preceding the beginning of treatment by several weeks or months. The patient, accompanied by the entourage of his choice, receives all information concerning the precise technical methods of treatment or proposed therapeutic combinations.The functional risks as well as the operational risk of death are stated repeatedly, in comparison to current knowledge on the natural history of intracerebral arteriovenous malformations. After this initial consultation, the patient has several months to reflect and possibly take other medical opinions. It is clearly explained to him that he does not have any obligation and that he always keeps, until the last moment, the total freedom to refuse the suggested therapeutic strategy without him being obliged to justify his refusal. In all the cases, the patient is informed of the priority given to the conservation of neurological function even if this may be done only at the price of a partial treatment. These consultations always end with the patient signing a document in which it is stated that he has received all information concerning the suggested therapeutic strategy and that he has been able to ask the neuroradiolo-

gist all the questions he wished. This document ends with the signature of agreement of the patient for the suggested strategy even if this entails therapeutic abstention.

Treatment technique

Of course, the strategic proposal, must take into account multiple parameters among which are the clinical history and the angioarchitecture of the arteriovenous malformation: topography – size – accessibility – feeding arteries and draining veins characteristics – general hemodynamic…). Patient personality is for us a paramount factor and particularly his psychological attitude with respect to the arteriovenous malformation, his profession and his wishes compared to the various risks among which it will be necessary for him to choose. Once arteriovenous malformations with a primary indication for radiosurgery or neurosurgery are eliminated, suggested therapeutic strategy will be staged embolization by hyperselective catheterization with the number of stages depending on the arteriovenous malformation size. Bulky arteriovenous malformation are never treated in one session even if it appears technically possible. Experience indeed teached us that the risk of hemorrhagic complications increases indisputably with the importance of the embolisation carried out. Thus, this lead us to privilege the progressive treatment.

Hyperselective catheterization is carried out with the thinnest possible microcatheters, preferably flow dependent. The use of microguides, is reserved only for those cases where flow is insufficient to carry out hyperselective catheterization in a blocked flow situation, which is the ideal condition. The Magic 1,2 F (Balt) microcatheters were the most often used except in cases where the importance of arteriovenous shunts required the use of cyanoacrylates in high concentrations or the use of Onyx.

The choice of embolization material is done primarily between the cyanoacrylates and Onyx. This is not the place to develop argumentation in favour of either products, but, obviously for historical reasons, in the majority of the cases of this work, embolizations were carried out using cyanoacrylates; only forty patients were embolized using Onyx.

Time interval between two embolizations varies from a few weeks to several months.This interval allows the patient to carry on a normal personal and professional life and, on the technical level, allows residual pedicles to gradually dilate and facilitate later approaches to the residual angiomatous nidus and consequently augments the efficiency of later embolizations.

Radiotherapy

When it gets technically impossible to access and embolize residual malformations without a major risk of functional deficit or when the arteriovenous malformations is fed by a particularly functional pedicle and is consequently considered as dangerous (for example proximal or middle third of the anterior choroidal artery), embolization is complemented by radiosurgery carried out in stereotaxic conditions with a linear accelerator.

The choice of radiosurgery versus open skull surgery as a therapeutic complement, relies often on the patient's choice when the therapeutic team estimates that the two techniques have the same functional risks. In addition, when the residual nidus is located in a highly functional zone, the therapeutic team generally prefers radiotherapy to surgery; an attitude that indisputably limits the risk of functional deficits.

Demarcation of the target is a particularly delicate and significant process, always carried out by the interventional neuroradiologist who carried out the initial embolizations. He is obviously the specialist who knows better the angioarchitecture of the malformation and consequently has the best knowledge to demarcate the irradiated territory. Demarcation of the target is carried out by superposition of 2D angiography on 3D angiography, as with a 3D angio MRI. This requires significant computer power, a subject that can not be described or detailed in this work. Demarcation and delivered radiation dose constitute significant parameters on which depends treatment success. In some cases, two or more exceptionally 3 targets, may be necessary: these will be irradiated in one or two sessions according to their respective topographic relations.

Results

Taking into account the extreme variety of arteriovenous malformations and consequently the practical impossibility to establish a worldwilde recognized classification system allowing valid comparisons, total results have only little

interest. However it is usefull to define cure criteria adopted on a radioanatomical and clinical level.

Anatomically, cure can be declared only on the basis of an excellent quality angiography carried out at distance, i.e. at least 6 months after the last therapeutic session: this assessment should show lack of arteriovenous shunts and absence of abnormal vascularization; in some cases, one may tolerate small residual vascular tortuosities without any abnormal arteriovenous communication. Of course this angiographic aspect has to remain stable in time.

Clinically, complete cure corresponds to a normal neurological and neurocognitive state, with the patient living a normal personal and professional life without any restriction. Persistence of an epilepsy, even perfectly controlled by medical treatment, is not compatible with the concept of complete cure, even if the patient has a "practically normal" life.

Globally, we first consider 517 patients who harbored a cortical arteriovenous supratentorial arteriovenous malformation, had undergone at least one treatment session and whose treatment was regarded as finished, excluding patients with deep arteriovenous malformations. Of these 517 patients, 336 i.e. 65% (64,99%) were regarded as radio anatomically cured. On the other hand, if the very strict criteria of clinical cure as defined above were applied, only 222 patients, that is 43% (42,94 %) were cured without sequellae.This holds in particular for the patients with persistent epilepsy, even when perfectly controlled by medical treatment.

The significant difference between the total number of patients and the number of patients retained for analysis, is due to the fact that a certain patients decided to stop their treatment before radioanatomical cure because "they fell well" and did not wish to take additional risks. These patients, who generally present and excellent clinical evolution, cannot of course be included in this statistical analysis.

An excellent example of this evolution is given by the AVMs of the corpus callosum which all extend widely along the corpus callosum. This is why this localization is recognized as particularly difficult "to cure". On a total of 42 patients, 35 AVMs, that is 83% had haemorrhage as the initial symptom: this is 2 times as high compared to the rate in our total population (37,6% of cases), confirming the notion of strong "hemorrhagic potential" of this localization. In this particular population, 2 patients died of spontaneous haemorrhage before the end of the treatment, 11 were clinically cured without any sequellae and 20 who were radioanatomically cured live a practically normal life presenting a rate of 73, 8%.

Complications

Embolization related complications are divided into two large categories according to their mechanism of occurence: hemorrhagic and ischaemic.

Hemorrhagic complications are the most serious ones. Estimation of their frequency varies, since small asymptomatic hemorrhages warrant systematic post embolization CT scans which are not always performed. Excluding small AVMs, it appeared to us that this frequency is related to the importance of the embolization performed as well as different parameters we have studied and published in 2001: multiplicity of feeding pedicles, lobar localisation and especially prolonged venous stagnation on the last angiographic control performed at the end of the embolization session.

Taking into account all these elements, of 728 embolized patients, 32 presented a post embolisation haemorrhage corresponding to a total rate of 4,39%. Among these 32 patients, 15 patient, that is 2,06% of the embolized total population, were completely asymptomatic: these were hemorrhages, sometimes within the limits of visibility, discovered on a systematic CT scan. The 17 remaining patients (2,33%) correspond to real hemorrhagic complications:10 surgically evacuated hematomas. *Globally*, 7 patients died: thus post embolisation mortality is 0,96%.Clinical evolution was extremely favorable for 5 patients while 7 presented neurological sequellae.

Experience has shown us that it is frequently possible to avoid these post embolization haemorrhages by inducing hypotension during the procedure prolonged for 3 days after the embolization. Indeed during the last 4 years, when embolization conditions or the last angiographic control make us fear a hemorrhagic complication, induction of hypotension during the procedure practically always allowed us to avoid a haemorrhage.This thus raises the question: should hypotension be systematically induced post embolization?

Ischemic complications are less frequent and

practically always predictable as they generally correspond to the occlusion of healthy territories arround the nidus. Here again the notion of ischemic complication has to be defined.It relates to embolization followed by clinical neurological deficits explained by iatrogenic ischemia visualized on post-procedural CT or MRI. Clinically, these neurological symptoms, mostly deficits, have to be distinguished from clinical degradations due to oedema, most often totally regressive, that may be encountered after embolization. If these criteria are respected, 11 patients out of 728, that is 1,5% presented an ischaemic complication.

Globally, of 728 patients followed during these 20 years, 27 died of a hemorrhagic accident, that is 3,70%. If one excludes 7 patients directly deceased because of an hemorrhagic complications due to the embolization, the mortality due to spontaneous hemorrhage during this long period of follow up is 20/720 that is 2,74%.

Conclusions

Treatment of AVMs, is of course associated to difficulties and complications that may sometimes be serious. But instead of obnubilating onself by comparing statistics of treatment complication rates and rates spontaneous undesirable events during the natural history of the disease, it is advisable to consider the positive evolution of completely cured patients and the cohort of patients the treatment helps to carry on a normal life.

The therapeutic philosophy we have developed consists, of course, in an attempt to completely eradicate the hemorrhagic risk by total and definitive radioanatomical cure of the malformation whenever possible, without too important neurologica deficits. If this is not achievable, we believe that partial treatment is a valuable alternative, especially if one has succeeded to eradicate the “weak points” of the malformation: intranidal aneurysms - high flow arteriovenous shunts...

It is finally advisable to specify that this therapeutic strategy is implemented allowing patients to live a nearly normal personal and professional life. We only recommend to avoid prolonged exposures to the sun as well as combat or competitive sports. Furthermor, in this population, 69 women concluded a pregnancy with childbirth by caesarean section, without any haemorrhagic episode. Three women bled during their pregnancy but, in these three cases, haemorrhages occurred before the endovascular treatment had begun.

Still remains regulation of what we could call the social and socio-economical consequences of the disease. Indeed, Insurance companies and Banks demand more and more medical information to those who wish to contract an insurance policy or obtain a bank loan. Completely cured patients who declare having been treated for an intracerebral arteriovenous malformation automatically see their premiums rise, which is a completely unjustified major handicap. This constitutes a true problem, particularly difficult to solve.

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Prof. L. Picard, MD
CHU Hopital Central
Service de Neuroradiologie
29, Av. Maréchal de Lattre deTassigny
F 54035 NANCY Cédex, France